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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,516	02/11/2005	Hans Loibner	4518-0109PUS1	1154

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EXAMINER	
SANG, HONG	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
06/13/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/524,516	LOIBNER ET AL.	
	Examiner	Art Unit	
	HONG SANG	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *6,9-22 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7, 8 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RE: Loibner et al.

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/6/2008 has been entered.

2. Claims 1-24 are pending. Claims 6, 9-22 and 24 have been withdrawn from consideration as being drawn to non-elected inventions.

3. Claims 1-5, 7, 8 and 23 are under examination. Due to restriction/species election, claims 5, 7, 8 and 23 are examined to the extent that antigen (a) is EpCAM, and antigen (b) is Lewis Y.

Claim Amendment

4. The amendment to the claims filed on 5/6/2008 does not comply with the requirements of 37 CFR 1.121(c) because applicants fail to rewrite the entire claim for claim 6. Amendments to the claims filed on or after July 30, 2003 must comply with 37 CFR 1.121(c) which states:

> (c) *Claims*. Amendments to a claim must be made by rewriting the entire claim with all changes (*e.g.*, additions and deletions) as indicated in this subsection, except when the claim is being canceled. Each amendment document that includes a change to an existing claim, cancellation of an existing claim or addition of a new claim, must include a complete listing of all claims ever presented, including the text of all pending and withdrawn claims, in the application. The claim listing, including the text of the

claims, in the amendment document will serve to replace all prior versions of the claims, in the application. In the claim listing, the status of every claim must be indicated after its claim number by using one of the following identifiers in a parenthetical expression: (Original), (Currently amended), (Canceled), (Withdrawn), (Previously presented), (New), and (Not entered).

(1) *Claim listing.* All of the claims presented in a claim listing shall be presented in ascending numerical order. Consecutive claims having the same status of "canceled" or "not entered" may be aggregated into one statement (*e.g.*, Claims 1–5 (canceled)). The claim listing shall commence on a separate sheet of the amendment document and the sheet(s) that contain the text of any part of the claims shall not contain any other part of the amendment.

(2) *When claim text with markings is required.* All claims being currently amended in an amendment paper shall be presented in the claim listing, indicate a status of "currently amended," and be submitted with markings to indicate the changes that have been made relative to the immediate prior version of the claims. The text of any added subject matter must be shown by underlining the added text. The text of any deleted matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show deletion of five or fewer consecutive characters. The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived. Only claims having the status of "currently amended," or "withdrawn" if also being amended, shall include markings. If a withdrawn claim is currently amended, its status in the claim listing may be identified as "withdrawn—currently amended."

(3) *When claim text in clean version is required.* The text of all pending claims not being currently amended shall be presented in the claim listing in clean version, *i.e.*, without any markings in the presentation of text. The presentation of a clean version of any claim having the status of "original," "withdrawn" or "previously presented" will constitute an assertion that it has not been changed relative to the immediate prior version, except to omit markings that may have been present in the immediate prior version of the claims of the status of "withdrawn" or "previously presented." Any claim added by amendment must be indicated with the status of "new" and presented in clean version, *i.e.*, without any underlining.

(4) *When claim text shall not be presented; canceling a claim.*

(i) No claim text shall be presented for any claim in the claim listing with the status of "canceled" or "not entered."

(ii) Cancellation of a claim shall be effected by an instruction to cancel a particular claim number. Identifying the status of a claim in the claim listing as "canceled" will constitute an instruction to cancel the claim.

(5) *Reinstatement of previously canceled claim.* A claim which was previously canceled may be reinstated only by adding the claim as a "new" claim with a new claim number.

Objections Maintained

5. The objection to claims 1-5, 7, 8 and 23 because the claims contain non-elected inventions such as antibody, non-elected antigens NCAM, CEA, Lewis b, sialyl-Tn, and Globe H is maintained.

The response states that the restriction requirement is an improper attempt to limit applicants to a species and is an improper application of the procedure for examination of generic and Markush-type claims.

Applicant presented same arguments as before, and these arguments have been responded in the previous office action. The rejection is maintained for the reasons of record.

Response to Arguments

Claim Rejections - 35 USC § 103

6. The rejection of claims 1-5, 7, 8 and 23 under 35 U.S.C. 103(a) as being unpatentable over WO 01/35989A2 (Pub. Date: 5/25/2001, IDS) (English translation CA 2391927) in view of Maruyama et al. (Cancer Immunol Immunother., 2000, 49: 123-132), Sabbatini et al. (Int. J. Cancer, 2000, 87: 79-85), and Berthelsen et al. (US Patent No. 6,455,290B1, Date of Patent 9/24/2002, effective filing date 7/9/1999) is maintained.

Applicants presented several arguments and each argument is addressed below:

Argument I: The prior art teaches away from the present invention.

Specifically applicants argued that combination of tumor antigens have problems such as cross-reactivity, and the use of an antigen in a therapy can be problematic over the use of anti-idiotypic antibody.

Applicant's arguments have been carefully considered but are not persuasive. The use of a vaccine comprising two or more tumor-associated antigens is well known in the art, as evidenced by Spitler (US Patent NO. 5,738,867, 4/14/1998). Spitler teaches that the antitumor vaccine compounds may be employed in cocktails of two or more different TAAs encapsulated in and/or conjugated to liposomes, and such cocktails may be of particular in certain highly metastatic cancers (see the paragraph bridging columns 4 and 5). Bystryn (US 5,030,621, Date of Patent: 7/9/1991) teaches treating cancer using a vaccine comprising a mixture of cancer cell-shed antigens (multiple melanoma associated antigens (MAAs) (see column 8, lines 31). Bystryn teaches that a mixture of tumor antigens in the vaccine would be appropriate to circumvent antigenic heterogeneity among melanomas (see column 8, lines 37-40). The cited reference Maruyama teaches that the native antigen GA733 (EpCAM) is superior to that of the anti-idiotypic antibody (Ab2) which mimicking a single EpCAM epitope (see abstract). Furthermore, both EpCAM antigen and Lewis y antigens have been successfully used in the prior art as a vaccine for treating cancer. Maruyama et al. teach a cancer vaccine comprising the antigen GA733 (EpCAM). Sabbatini et al. teach a vaccine comprising Lewis y antigen for treating ovarian cancer (see abstract). While neither Maruyama nor Sabbatini teaches a vaccine comprising both EpCAM and Lewis y antigens, the use of these two antigens together is obvious in view of the teachings of

WO 01/35989A2. WO 01/35989A2 teaches a pharmaceutical composition (vaccine) comprising anti-idiotypic antibody for EpCAM, anti-idiotypic antibody for Lewis Y, or anti-idiotypic antibodies for both EpCAM and Lewis Y antigens (see page 7, Examples 1-7, and claim 16). WO 01/35989A2 teaches that within an immunologic meaning, some anti-idiotypic antibodies can represent the "internal image" of an antigen, such antibodies may therefore be used, as a vaccine, for inducing an immune response in cancer patients, said immune response being possibly directed against said tumor-associated antigen (see page 2, 3rd paragraph and page 3, lines 3-6 of CA 2391927). Therefore, WO 01/35989A2 teaches that antigenic mimics of EpCAM and Lewis y can be used together for treating cancer. In view of the teachings of WO 01/35989A2, Maruyama, Sabbatini, and state of the prior art, one skilled in the art would expect that EpCAM and Lewis y antigens can be used together for treating cancer given the fact that they induce immune response to the same proteins i.e. EpCAM and Lewis y as their anti-idiotypic antibodies do. Furthermore, Maruyama et al. teach that the immunomodulatory activity of the native antigen GA733 (EpCAM) is superior to that of the anti-idiotypic antibody (Ab2) which mimicking a single EpCAM epitope (see abstract). One would have been motivated to use the native antigen GA733 instead of its anti-idiotypic antibody. One of ordinary skill in the art would have a reasonable expectation of success to make the vaccine of GA733 and Lewis y antigen because each of the antigens is known in the art and has been prepared as a cancer vaccine.

With respect to applicant's arguments that Luo' and Kieber-Emmons's references disclose that carbohydrate Lewis Y is generally problematic for induction of a T-cell

dependent immune response, and consequently the use of peptide/protein mimics (including anti-idiotypic antibodies) would be the primarily preferred way to go base on the state of the art, this argument is not persuasive. As indicated in the previous office action, the cited reference Sabbatini et al. explicitly concludes based on a phase 1 trial study that LeY-KLH should be a suitable component for a polyvalent vaccine under consideration for the therapy of epithelial cancers (see abstract). Moreover, Maruyama teaches that the native antigen GA733 (EpCAM) is superior to that of the anti-idiotypic antibody (Ab2) which mimicking a single EpCAM epitope (see abstract). Maruyama further teaches that soluble antigen is a more potent modulator of humoral and cellular immune response than Ab2 (see abstract). Therefore, the prior art does not teach away from the instant invention.

Argument II: The invention demonstrates new and unexpected results relative to the prior art.

Specifically applicants pointed to Figure 4 in the specification to show unexpected results.

Applicant's arguments have been carefully considered but are not persuasive. Figure 4 in the specification shows results of an antibody dependent cellular cytotoxicity assay wherein SKBRE cells were treated with IGN311 (humanized anti-Lewis Y antibody, see specification page 29, line 6), Herceptin®, or a combinations thereof (see Figure 4 and page 21, 4th paragraph). These results do not provide evidence for unexpected results because Figure 4 uses antibodies, whereas the instant inventions

use tumor associated antigen. Moreover, the instant claims are directed to EpCAM antigen and Lewis Y antigen, Figure 4 is directed to Her2 (ErbB2) antibody and Lewis Y antibody. Therefore, Figure 4 does not provide support for unexpected results.

In view of above, the invention as a whole was deemed *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Therefore, the rejection is maintained.

It is noted that although the claims recite a kit, no positive recitation of the kit ingredients/ elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to place the recited elements in a kit for the advantages of convenience and economy. Thus, the claimed subject matter is considered obvious over the prior art, absent sufficient factual evidence to the contrary.

7. The rejection of claims 1-5, 7, 8 and 23 under 35 U.S.C. 103(a) as being unpatentable over Spitler (US Patent NO. 5,738,867, 4/14/1998) in view of Sabbatini et al. (Int. J. Cancer, 2000, 87: 79-85), and Berthelsen et al. (US Patent No. 6,455,290B1, Date of Patent 9/24/2002, effective filing date 7/9/1999) is maintained.

Applicants did not specifically argue this rejection. The rejection is maintained for the reasons of record, and those set forth above (see paragraph 6 above).

It is noted that although the claims recite a kit, no positive recitation of the kit ingredients/ elements distinguishes the claim over the references. Therefore, the references read on the claimed kit. Further, it is a well-known convention in the art to

place the recited elements in a kit for the advantages of convenience and economy. Thus, the claimed subject matter is considered obvious over the prior art, absent sufficient factual evidence to the contrary.

New Grounds of Rejections

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Marciani et al. (US 6,080,725, Date of Patent: 6/27/2000), as evidenced by Stocks et al. (Glycosylation & Disease, 1994, 1: 279-286)

Marciani et al. teach a vaccine comprising one or more tumor associated antigens (see claims 1 and 15), wherein the tumor associated antigens may be CEA, MUC-1, PSA, ovarian cancer antigen, EGFR, or mixtures thereof (see claim 16), wherein the tumor antigens can be native, recombinant or synthetic (see column 27, lines 31-52, and claim 17). Marciani et al. teach that the vaccine can be administered intravenously (see column 31, lines 4-5). Marciani et al. teach a kit for the immunization (see column 31, lines 31-37). It is known in the art that native tumor associated antigens are glycosylated, as evidenced by Stocks et al. Stocks et al. teach that CEA is

a heavily glycosylated protein (see page 280, 2nd paragraph). Therefore, the native tumor antigens would comprise at least one epitope of an aberrant protein glycosylation.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to HONG SANG whose telephone number is (571)272-8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Hong Sang/
Art Unit 1643
6/6/2008